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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/574,477

01/09/2007

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EXAMINER

KATAKAM, SUDHAKAR

ART UNIT

PAPER NUMBER

1621

MAIL DATE

DELIVERY MODE

02/12/2009

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/574,477	SUDOH ET AL.	
	Examiner	Art Unit	
	Sudhakar Katakam	1621	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 24 November 2008.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-3,5,7-16,18,19,23-31,33 and 34 is/are pending in the application.
- 4a) Of the above claim(s) 18,19 and 29-31 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-3,5,7-16,23-28,33 and 34 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>12/29/08</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Status of the application

1. Receipt of Applicant's request for continued examination filed on 24th Nov 2008 is acknowledged.

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 24th Nov 2008 has been entered.

Claim Rejections - 35 USC § 103

2. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

3. The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

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4. Claims 1-3, 5, 7-16, 23-28, and 33-34 are rejected under 35 U.S.C. 103(a) as being unpatentable over **Hasegawa et al** (Bull.Chem.Soc.Jpn. 2000, 73, 423-428) or **JP 8291106** in view of **Ohuchida et al** (US 6,201,021), **Black** (US 6,043,223), **Toda et al** (US 6,608,221) and **Takada et al** (US 2002/0022738 A1).

Hasegawa et al disclose an optically active (R)-2-propyloctanoic acid, valuable therapeutic agent for neurodegenerative diseases such as Alzheimer's disease (see equation 1 in page 423 and introduction).

JP 8291106 also discloses a salt of optically active (2R)-2-propyloctanoic acid for use in treating neurodegenerative disorders (see Abstract, translation is pending, and attached Derwent abstract).

The difference between the instant claims and the references is that the references teach the compound or it's salt and silent on the source of metal ion, pH and the concentration of the components in the medicament.

However, the source of metal ions is very well established in the art. The most common sources of metal ions in the art are di or tri-sodium phosphate, sodium or potassium hydroxide etc. One skilled person in the art would be motivated to choose a metal ion source as a matter of choice depending on variables such as compound solubility factors or availability or cost etc. Furthermore a person of ordinary skill has good reason to pursue the known options within his or her technical grasp. If this leads to the anticipated success, it is likely the product not of innovation but of ordinary skill and common sense. Applicants are invited to provide a showing which is

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commensurate in scope with the claimed invention that clearly demonstrate that the claimed metal ion source result in some unexpected property over the prior art.

There are many prior art available, which teaches the source of metal ions to stabilize the drug compounds. The following examples illustrate the multiple utilities of metal ion sources, such as sodium phosphate, for small peptides to drug compounds.

Black teaches use of phosphate buffer saline solution as a carrier for the bradykinin, comprises 10-40 micrograms/mL of bradykinin and 0.09% phosphate buffered saline solution [col. 5, lines 41-45]. **Black** also teaches infusion preparation of bradykinin that is dissolved in aqueous solution containing sodium hydroxide and phosphate buffered saline solution [col. 5, lines 47-62]. Preparation of infusions for drugs, such as (2R)-2-propyloctanoic acid, are known in the art. Also the process of adjusting pH using buffers is also very well known procedure in the art.

Toda et al teach that (2R)-2-propyloctanoic acid, which is produced after the reductive reaction, is extracted with sodium hydroxide, it is clear that the sodium salt found in (2R)-2-propyloctanoic acid is produced in this series [see example 1].

Ohuchida et al teach suitable basic metal ions for the preparation of salts of pentanoic acid derivatives [col.17, lines 1-24].

Takada et al teach a process to improve the solubility of the drug compound and thereby providing a solution thereof and some kinds of drug products using the solution, moreover providing a solution of higher concentration and a high-dosage drug product using the solution, and in order to improve the solubility of drug compounds, which can

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be accomplished by adding at least one pH adjuster selected from tri-sodium phosphate, a hydrate thereof, sodium hydroxide or potassium hydroxide to the solution [see 0008 - 0010].

The claims would have been obvious because, a person of ordinary skill has a good reason to pursue the known options within his or her technical grasp. If this leads to the anticipated success, it is likely the product, not of innovation, but of ordinary skill and common sense.

The claim would have been obvious because the design incentives or market forces provided a reason to make an adaptation, and the invention resulted from application of the prior knowledge in a predictable manner.

All the claimed elements were known in the prior art and one skilled person in the art could have combined the elements as claimed by known methods with no change in their respective functions, and the combination would have yielded predictable results to have yielded predictable results to one of ordinary skill in the art at the time of the invention.

The Supreme Court in KSR noted that if the actual application of the technique would have been beyond the skill of one of ordinary skill in the art, then the resulting invention would have been obvious because one of ordinary skill could not have been expected to achieve it.

Therefore, it would have been obvious to a person of ordinary skill in the art at the time of the invention to use the teachings of the above cited references and known

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methods, to make the composition of (2R)-2-propyloctanoic acid with basic metal ions, from the art, and to make the instant applicants medicament with a reasonable expectation of success. One would have been motivated to arrive instant claims because **Hasegawa et al** teach “preparation of (2R)-2-propyloctanoic acid” and this compound is a therapeutic agent of neurodegenerative diseases such as Alzheimer’s disease. **Takada et al** teach a process to improve the solubility of the drug compound using the sodium phosphate. Therefore, one would combine the teachings of the references in order to provide for a medicament mixing the (2R)-2-propyloctanoic acid with a basic metal ion to facilitate the better stability of the drug composition in storage. For the foregoing reasons the instant claims are made obvious.

Modifying such process is prima facie obvious because an ordinary artisan would be motivated to explore the known metal ions sources from the art to make the drug composition more stable or more economical advantages over the other, since it is within the scope to optimize the conditions through a routine experimentation.

Response to Arguments

5. Applicant’s arguments filed on 24th Nov 2008 have been fully considered but they are not persuasive.

The examiner acknowledges applicants argument that the **Black** is not related to the present invention and can not be combined with the other cited references as suggested by the examiner.

The examiner contends, however, that the purpose of **Black** is to show the applicants the use of metal ions sources, such as sodium phosphate, to stabilize the

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drug compounds or peptides. Therefore, it is appropriate in combination with the other references.

The examiner acknowledges applicant argument that "it cannot be said that the composition of the present invention is obvious based on the disclosure of a combination of the cited references, which relates to an infusion preparation for a compound which has a much different molecular weight and different features of its liquid composition".

The examiner contends, however, the obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988) and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). In this case, it is permissible for the examiner to rely on disclosures and known metal ions sources in the art, which fairly teach embodiments of applicant's invention. The claims require a multitude of elements and it is reasonable for one of ordinary skill in the art to consider these elements being used together.

Applicants show how the cited references differ from the instant invention, but the obviousness test under 35 U.S.C. 103 is whether the invention would have been obvious in view of the prior art taken as a whole. *In re Metcalf et al.* 157 U.S.P.Q. 423.

So, it would have been obvious to a person of ordinary skill in the art at the time of the invention was made, with the teachings of the cited reference to make applicants'

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claimed medicament with a reasonable expectation of success, since it is within the scope to optimize the conditions through a routine experimentation.

Conclusion

6. No claim is allowed.

7. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sudhakar Katakam whose telephone number is 571-272-9929. The examiner can normally be reached on M-F 8:30 AM - 5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Daniel Sullivan can be reached on 571-272-0779. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Peter G O'Sullivan/
Primary Examiner, Art Unit 1621

/Sudhakar Katakam/
Examiner, Art Unit 1621